Poster Presentation

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Structural studies of anti-IgE Fab fragments

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In recent decades, the incidence of allergy, an immune disorder mediated by immunoglobulin E (IgE), has increased [1]. In Europe alone, allergic rhinitis and asthma affect 113 and 65 million people respectively [2]. The symptoms of these diseases not only cause discomfort to patients but also may be fatal, especially in asthmatic sufferers. Although the aetiology of allergy is debated, it is widely accepted that the interaction of IgE with its high-affinity receptor (FcεRI) is directly implicated to the pathogenesis of allergy [1]. The treatments for allergy include antihistamines and/or bronchodilators, for symptomatic relief, or corticosteroids to prevent the onset of symptoms. However, none of these medications are direct modulators of allergy. The most effective therapeutic for asthma is omalizumab, a monoclonal anti-IgE antibody. Omalizumab, an IgG1 antibody, prevents the allergic response by inhibiting the binding of IgE to FcεRI. The exact mechanism of action of omalizumab is yet to be defined, but it inhibits the IgE/FcεRI protein-protein interaction. Studies on the interaction of omalizumab Fab with IgE are crucial to reveal the binding site. We report here the structures of omalizumab Fab and two different Fab mutants in different crystal forms, and examine the effect of packing on the structure. We observed conformational changes in the complementarity-determining regions (CDRs) between the mutants compared with wild-type Fab. Side-chain conformational changes associated with the different crystal packings were also observed among the six different crystal structures.

[1] *Gould, H.J. and B.J. Sutton, IgE in allergy and asthma today. Nat. Rev. Immunol., 2008. 8(3): p. 205-17.,* ***[2]*** *Asher, M.I., et al., Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet, 2006. 368(9537): p. 733-43.*

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